CLAIMS

We claim:

1. A polypeptide having the structure X-Y wherein X is selected from the group consisting of an Ala residue and heterologous peptides capable of adopting a stable secondary structure and Y is a soluble CD39 polypeptide selected from the group consisting of:

(a) polypeptides having an amino acid sequence as set forth in Figure 1 (SEQ ID NO:2) wherein the amino terminus is selected from the group consisting of amino acids 36-44, and the carboxy terminus is selected from the group consisting of amino acids 471-478;

(b) fragments of the polypeptides of (a) wherein said fragments have apyrase activity; and

(c) variants of the polypeptides of (a) or (b), wherein said variants have apyrase activity.

2. The polypeptide of claim 1 wherein Y is a soluble CD39 polypeptide selected from the group consisting of:

(a) polypeptides having a sequence consisting of amino acids 38-476 or 39-476 of SEQ ID NO:2;

(b) variant polypeptides that are at least 70% identical in amino acid sequence to amino acids 36 to 478 of SEQ ID NO:2 or to a fragment thereof, wherein said variant polypeptides have apyrase activity;

(c) variant polypeptides that are at least 80% identical in amino acid sequence to amino acids 36 to 478 of SEQ ID NO:2 or to a fragment thereof, wherein said variant polypeptides have apyrase activity;

(d) variant polypeptides that are at least 90% identical in amino acid sequence to amino acids 36 to 478 of SEQ ID NO:2 or to a fragment thereof, wherein said variant polypeptides have apyrase activity;

(e) variant polypeptides that are at least 95% identical in amino acid sequence to amino acids 36 to 478 of SEQ ID NO:2 or to a fragment thereof, wherein said variant polypeptides have apyrase activity;

(f) variant polypeptides that are at least 98% identical in amino acid sequence to amino acids 36 to 478 of SEQ ID NO:2 or to a fragment thereof, wherein said variant polypeptides have apyrase activity; and

(g) variant polypeptides that are at least 99% identical in amino acid sequence to amino acids 36 to 478 of SEQ ID NO:2 or to a fragment thereof, wherein said variant polypeptides have apyrase activity.

3. The polypeptide of claim 1 wherein X is a peptide fragment from the amino terminal portion of mature IL-2, CD39-L2, CD39-L3, or CD39-L4.

4. A polypeptide having the structure A-B-Y wherein A is 0-20 amino acids from the amino terminal portion of mature IL-2, B is a linker of 0-15 amino acids, and Y is a soluble CD39 polypeptide selected from the group consisting of:

(a) polypeptides having an amino acid sequence as set forth in Figure 1 (SEQ ID NO:2) wherein the amino terminus is selected from the group consisting of amino acids 36-44, and the carboxy terminus is selected from the group consisting of amino acids 471-478;

(b) fragments of the polypeptides of (a) wherein said fragments have apyrase activity; and

(c) variants of the polypeptides of (a) or (b), wherein said variants have apyrase activity.

5. A soluble CD39 polypeptide comprising a sequence selected from the group consisting of:

(a) SEQ ID NO: 6, amino acids 25-464 of SEQ ID NO:27, amino acids 25-474 of SEQ ID NO:28, amino acids 27-473 of SEQ ID NO:29, amino acids 21-476 of SEQ ID NO:3, amino acids 21-476 of SEQ ID NO:4, or amino acids 21-463 of SEQ ID NO:30; and

(b) fusion polypeptides comprising the polypeptides of (a), wherein said fusion polypeptides have apyrase activity.

6. The soluble CD39 polypeptide of claim 5 having an amino acid sequence selected from the group consisting of SEQ ID NO: 6, amino acids 25-464 of SEQ ID NO:27, amino acids 25-474 of SEQ ID NO:28, amino acids 27-473 of SEQ ID NO:29, amino acids 21-476 of SEQ ID NO:3, amino acids 21-476 of SEQ ID NO:4, and amino acids 21-463 of SEQ ID NO:30.

7. The soluble CD39 polypeptide of claim 6 having the sequence of amino acids 21-463 of SEQ ID NO:30.

8. An isolated nucleic acid encoding a polypeptide of claim 1.

9. The nucleic acid of claim 8 wherein said nucleic acid is DNA.

10. The DNA of claim 9 having a sequence selected from the group consisting of:

(a) SEQ ID NO:5; and

(b) DNA sequences which, due to degeneracy of the genetic code, encode the polypeptide encoded by SEQ ID NO:5.

11. The DNA of claim 9 wherein said DNA further encodes a leader peptide operably linked to the N-terminus of the polypeptide, wherein the leader peptide facilitates the extracellular secretion of the polypeptide.

12. The DNA of claim 11 wherein the leader peptide comprises all or part of a leader from IL-2, proinsulin, human growth hormone (huGH), IL7, or Igkappa.

13. The DNA of claim 12 wherein the leader peptide comprises the sequence SEQ ID NO:9.

14. The DNA of claim 11 having a sequence selected from the group consisting of

(a) SEQ ID NO:7; and

(b) DNA sequences which, due to degeneracy of the genetic code, encode the polypeptide encoded by SEQ ID NO:7.

15. A vector comprising the nucleic acid of claim 8.

16. The vector of claim 15 wherein said vector is a eukaryotic expression vector.

17. A recombinant cell comprising the nucleic acid of claim 8.

18. The cell of claim 17 wherein said cell is a prokaryotic cell.

19. The cell of claim 17 wherein said cell is a eukaryotic cell.

20. The cell of claim 19 wherein said cell is a COS cell or a CHO cell.

21. The cell of claim 20 wherein said cell is a CHO cell that has been adapted to grow in suspension and in the absence of serum.

22. A process for preparing a soluble CD39 polypeptide comprising culturing a recombinant cell according to claim 17 under conditions that permit expression of the CD39 polypeptide and recovering the CD39 polypeptide from the culture.

23. The process of claim 22 wherein the recombinant cell is a eukaryotic cell.

24. The process of claim 22 wherein the recombinant cell is a CHO cell that has been adapted to grow in suspension and in the absence of serum.

25. A polypeptide produced according to the process of claim 22.

26. A polypeptide produced according to the process of claim 24.

27. A composition comprising a pharmaceutically acceptable carrier and a polypeptide according to claim 1.

28. A composition comprising a pharmaceutically acceptable carrier and a polypeptide according to claim 5.

29. A composition comprising a pharmaceutically acceptable carrier and a polypeptide according to claim 25.

30. A method of inhibiting angiogenesis in a mammal in need of such treatment comprising administering a therapeutic amount of a soluble CD39 polypeptide.